

### REMARKS

Claims 9, 16, and 24-30 are pending in the present application. Claims 9 and 16 have been amended; claims 1-8, 10-15 and 17-23 have been cancelled; and new claims 24-30 have been added. New claims 24-28 belong to the elected restriction Group VI. New claims 29 and 30 belong to the same Group as claim 16, which was withdrawn by the Examiner after applicants' election of Group VI, leaving claims 9 and 24-27 under consideration. Support for these amendments can be found throughout the application as filed, including at page 6, lines 3-22; page 6, line 29 to page 7, line 6; page 8, lines 9-21; page 9, lines 14-27; and the claims as filed. No new matter has been added.

#### *Claim Objections*

Claims 9 and 10 were objected to for depending on non-elected claims 1 and 2, and for including multiple inventions. Claim 10 has been cancelled, thereby obviating the rejection as to that claim. The subject matter of original claim 9 (as it depended from claim 1) now appears in claims 9, 26, and 28, each of which reflects the election of SEQ ID NO:4. Applicants request that the objection to the claims be withdrawn in light of these amendments.

#### *Priority*

Applicants submit herewith a certified translation of the priority document, Japanese Patent Application No. JP 11/118806, filed on 04/26/1999, in compliance with 37 CFR § 1.55. Applicants submit that this perfects the claim of priority in this application.

#### *Claim Rejections – 35 U.S.C. § 112*

Claim 9 was rejected under the second paragraph of 35 U.S.C § 112 as allegedly indefinite due to the recitation of “under stringent conditions.” The relevant subject matter is deleted from claim 9 and now appears in claim 28. As claim 28 sets forth appropriate hybridization conditions, applicants request withdrawal of this rejection.

Claim 9 was also rejected under the first paragraph of 35 U.S.C § 112 as allegedly lacking written description support, as the scope of the claims included polypeptides encoded by

nucleic acids comprising less than the full open reading frame without specifying a correlated function (see pages 4-5 of the Office Action).

Applicants submit that the claims as amended meet the written description requirement. The subject matter of original claim 9 now appears in claims 9, 26, and 28 and their dependent claims. The Examiner noted that "substantially purified polypeptides comprising SEQ ID NO:4," as recited in claim 26, meets the written description requirement. Thus, the rejection should not be applied to claim 26.

Claims 9, 24 and 25 also have written description support. Once a sequence (such as SEQ ID NO:4) is determined, one of ordinary skill would be able to describe all possible variants containing ten or fewer conservative substitutions.

Claim 9 has been amended to specify a polypeptide comprising the amino acid sequence of SEQ ID NO:4, in which ten or fewer amino acids are conservatively substituted, wherein the polypeptide has a cellular proliferation inhibitory activity. In claim 9, the number of variants is limited by the requirement that the polypeptides have ten or fewer conservative substitutions in SEQ ID NO:4; one of skill in the art would appreciate that a number of conservative substitutions could be made that would be unlikely to affect the function of the polypeptide. The species disclosed are representative of the genus because all members differ from the reference compound by only ten or fewer conservative amino acid substitutions. One of skill in the art would conclude that applicants were in possession of the necessary common attributes possessed by the members of the genus.

Indeed, the written description guidelines recognize that claims drafted to cover variants can meet the written description requirement (see, e.g., "Example 14: Product by Function" of the Synopsis of Application of The Written Description Guidelines). In accordance with that example of the guidelines, applicants have included in claim 9 (and thus in claims 24 and 25 dependent therefrom) a functional limitation: the claimed polypeptide must have a cellular proliferation inhibitory activity. The specification also includes assays for identifying all of the variants of SEQ ID NO:4 that are capable of the specified cellular proliferation inhibitory activity (see Example 8). Mutants lacking activity are also identified (see Example 8).

Following the logic of the Written Description Guidelines, claims 9, 24 and 25 are amply supported in the specification.

Finally, claim 28 is drawn to a genus of polypeptides encoded by nucleic acids that must hybridize under highly stringent conditions with a probe consisting of the complement of SEQ ID NO:3, and must encode a polypeptide with a defined activity. "Example 9: Hybridization" of the Synopsis of Application of The Written Description Guidelines is relevant:

...a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

Although this Example relates to a nucleic acid claim, it is equally applicable to claim 28. Variation among the species of polypeptides is limited by the stringent hybridization conditions, which would produce structurally similar DNAs. One of skill in the art would appreciate that structurally similar DNAs would, in turn, encode structurally similar polypeptides. Assays for identifying all of the variants of SEQ ID NO:4 that are capable of the specified cellular proliferation inhibitory activity are disclosed (see Example 8). One of skill in the art would conclude that applicants were was in possession of the necessary common attributes possessed by the members of the genus. Therefore, Applicants submit that all of the claims amended meet the written description requirement.

Claims 9 and 10 were rejected as allegedly lacking enablement for "fragments and mutants for anti-growth activity" (see the Office Action at page 6). Claim 10 has been cancelled. Claim 9 has been amended as described above. Applicants submit that, as it would require no more than routine experimentation to make the polypeptides recited in amended claim 9 and new claims 24-28 and test them for cell proliferation inhibitory activity, claim 9 as amended and new claims 24-30 are fully enabled.

For at least the above reasons, Applicants request withdrawal of the rejections under 35 U.S.C. § 112.

*Claim Rejections – 35 U.S.C. § 102*

Claim 9 was rejected as anticipated by Wassenhove-McCarthy et al., J. Biol. Chem. 274:25004-25017 (August 27, 1999). As noted above, Applicants submit herewith a certified translation of the priority document, Japanese Patent Application No. JP 11/118806, filed on 04/26/1999, which was before the effective date of the Wassenhove-McCarthy reference. The priority document disclosed the claimed polypeptide sequences (see the Sequence listing attached to the priority document), thereby obviating the rejection (as the Examiner notes at page 9 of the Office Action).

Claim 9 was additionally rejected as anticipated by Daigo et al., Cancer Research 159:1966-1972 (April 15, 1999), which had two amino acids ("PD") in common with the claimed polypeptides, and WO 89/04875 (June 1, 1989), which had five amino acids ("GPPAA") in common with the claimed polypeptides. The claims have been amended to exclude these sequences.

Applicants submit that the claimed polypeptides are novel and request withdrawal of the rejection under 35 U.S.C. § 102.

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*Conclusion*

For at least the above reasons, Applicants submit that the claims as amended are patentable and request rapid allowance of the same. If the Examiner feels that a telephone conversation would be helpful in advancing prosecution of this application, the Examiner is invited to telephone the undersigned at 617-542-5070.

Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 14875-091001.

Respectfully submitted,

Date: 12/23/04

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